IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

van der Kuyl et al.

Serial No.: To be assigned

Filed: January 23, 2002

For: MEANS AND METHODS FOR

TREATMENT EVALUATION

Examiner: To be assigned

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PRELIMINARY AMENDMENT

Commissioner for Patents Washington, D.C. 20231

Sir:

Before examination of the above entitled application, please amend the above identified patent application as follows:

IN THE CLAIMS:

Please amend claims as follows. Please note that claim amendments are presented here in clean form for clarity, a marked up version of the claim amendments is attached.

- 3. (Amended) The method according to claim 1, wherein said sample comprises at least one of said target cells.
- 4. (Amended) The method according to claim 1, wherein said sample is obtained within one week of initiating said treatment.
- 5. (Amended) The method according to claim 1, wherein said sample is obtained within two days of initiating said treatment.
- 6. (Amended) The method according to claim 1, wherein said marker gene comprises a gene involved in the generation, maintenance and/or breakdown of blood vessels.
- 7. (Amended) The method according to claim 1, wherein said marker gene comprises a sequence as depicted in Table 1 or Table 2.
- 8. (Amended) The method according to claim 1, wherein said marker gene comprises a sequence selected from the group consisting of a sequence depicted in Figure 1 through 18 or a part or analogue thereof.
- 9. (Amended) The method according to claim 1, wherein expression of said marker gene is quantified.
- 10. (Amended) The method according to claims 1, further comprising comparing expression of said marker gene with a reference value.
- 11. (Amended) The method according to claim 2, wherein said tumor comprises Kaposi's Sarcoma.

- 14. (Amended) The method according to claim 12, further comprising determining the presence of a tumor cell in an individual.
- 15. (Amended) The method according to claim 12, further comprising determining the presence of a site of angiogenesis in an individual.
- 16. (Amended) The method according to claim 12, further comprising determining whether a treatment is effective in changing the status of a certain set of target cells in an individual.
- 17. (Amended) The method according to claim 12, further comprising determining whether a treatment is effective in counteracting a tumor in said individual.
- 18. (Amended) The method according to claim 14, wherein said tumor comprises Karposi's Sarcoma.
- 23. (Amended) The method according to claim 21, wherein said gene comprises a sequence selected from the group consisting of a sequence as depicted in Figure 1-18, a sequence as depicted in Table 1, a sequence as depicted in Table 2, or a part or analogue thereof.
- 24. (Amended) The method according to claim 21, wherein said hemopoietic cell comprises a peripheral blood mononuclear cell.
- 27. (Amended) The method according to claim 25, wherein said marker gene comprises a sequence selected from the group consisting of a sequence as depicted in Figure 1-18, a sequence as depicted in Table 1, a sequence as depicted in Table 2, or a part or analogue thereof.
- 28. (Amended) The method according to claim 25, wherein said treatment involves the use of at least one drug selected from the group consisting of 2ME2, Angiostatin, Angiozyme, Anti-VEGF RhuMAb, Apra (CT-2584), Avicine, Benefin, BMS275291, Carboxyamidotriazole,

CC44047, CC5013, CC7085, CDC801, CGP-41251 (PKC 412), CM101, Combretastatin A-4 Prodrug, EMD 121974, Endostatin, Flavopiridol, Genistein (GCP), Green Tea Extract, IM-862, ImmTher, Interferon alpha, Interleukin-12, Iressa (ZD1839), Marimastat, Metastat (Col-3), Neovastat, Octreotide, Paclitaxel, Penicillamine, Photofrin, Photopoint, PI-88, Prinomastat (AG-3340), PTK787 (ZK22584), RO317453, Solimastat, Squalamine, SU 101, SU 5416, SU-6668, Suradista (FCE 26644), Suramin (Metaret), Tetrathiomolybdate, Thalidomide, TNP-470, and Vitaxin.

- 29. (Amended) The method according to claim 1, wherein said sample is a blood sample.
- 30. (Amended) The method according to claim 1, wherein said sample comprises a peripheral blood mononuclear cell.
- 31. (Amended) The method according to claim 1, wherein said expression product comprises one of a TIE 1 sequence, a Salioadhesion or Siglec 1 sequence, a sequence as depicted in Figure 8 or Figure 17, or a part of analogue thereof.
- 37. (Amended) A method of determining whether a treatment is effective in changing the status of a certain set of target cells in an individual and/or altering an angiogenic process in an individual, said method comprising: providing the diagnostic kit according to claim 35; obtaining a sample from said individual; and detecting the presence of an expression product of at least one marker gene in said sample.
- 38. (Amended) A method of determining whether an individual possesses a tumor cell and/or a site of angiogenesis, said method comprising: providing the diagnostic kit according to claim 35; obtaining a sample from said individual; and quantifying an expression product of at least one marker gene in said sample.

Remarks

The Office is respectfully requested to enter the above amendments prior to the calculation of the filing fee in this application. The amendments and claim cancellations are made without prejudice or disclaimer. The amendments merely remove multiple dependencies. Should the Office determine that additional issues remain which might be resolved by a telephone conference, it is respectfully invited to contact applicants' undersigned attorney.

Respectfully Submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please amend the claims as follows:

- 3. (Amended) The method according to claim 1[or 2], wherein said sample comprises at least one of said target cells.
- 4. (Amended) The method according to <u>claim 1</u>[any one of claims 1-3], wherein said sample is obtained within one week of initiating said treatment.
- 5. (Amended) The method according to <u>claim 1</u>[any one of claims 1-4], wherein said sample is obtained within two days of initiating said treatment.
- 6. (Amended) The method according to <u>claim 1</u>[any one of claims 1-5], wherein said marker gene comprises a gene involved in the generation, maintenance and/or breakdown of blood vessels.
- 7. (Amended) The method according to <u>claim 1</u>[any one of claims 1-6], wherein said marker gene comprises a sequence as depicted in Table 1 or Table 2.
- 8. (Amended) The method according to <u>claim 1</u> [any one of claims 1-7], wherein said marker gene comprises a sequence selected from the group consisting of a sequence depicted in Figure 1 through 18 or a part or analogue thereof.
- 9. (Amended) The method according to <u>claim 1</u>[any one of claims 1-8], wherein expression of said marker gene is quantified.
- 10. (Amended) The method according to <u>claim 1</u> [any one of claims 1-9], further comprising comparing expression of said marker gene with a reference value.

- 11. (Amended) The method according to <u>claim 2</u> [any one of claims 2-10], wherein said tumor comprises Kaposi's Sarcoma.
- 14. (Amended) The method according to claim 12 [or claim 13], further comprising determining the presence of a tumor cell in an individual.
- 15. (Amended) The method according to claim 12 [or claim 13], further comprising determining the presence of a site of angiogenesis in an individual.
- 16. (Amended) The method according to claim 12 [or claim 13], further comprising determining whether a treatment is effective in changing the status of a certain set of target cells in an individual.
- 17. (Amended) The method according to <u>claim 12</u>[any one of claim 12-16], further comprising determining whether a treatment is effective in counteracting a tumor in said individual.
- 18. (Amended) The method according to claim 14 [or 17], wherein said tumor comprises Karposi's Sarcoma.
- 23. (Amended) The method according to claim 21 [or 22], wherein said gene comprises a sequence selected from the group consisting of a sequence as depicted in Figure 1-18, a sequence as depicted in Table 1, a sequence as depicted in Table 2, or a part or analogue thereof.
- 24. (Amended) The method according to <u>claim 22</u> [any one of claims 21-23], wherein said hemopoietic cell comprises a peripheral blood mononuclear cell.
- 27. (Amended) The method according to claim 25 [or 26], wherein said marker gene comprises a sequence selected from the group consisting of a sequence as depicted in Figure 1-18, a sequence as depicted in Table 1, a sequence as depicted in Table 2, or a part or analogue thereof.

- 28. (Amended) The method according to <u>claim 25</u>[any one of claims 25-27], wherein said treatment involves the use of at least one drug selected from the group consisting of 2ME2, Angiostatin, Angiozyme, Anti-VEGF RhuMAb, Apra (CT-2584), Avicine, Benefin, BMS275291, Carboxyamidotriazole, CC44047, CC5013, CC7085, CDC801, CGP-41251 (PKC 412), CM101, Combretastatin A-4 Prodrug, EMD 121974, Endostatin, Flavopiridol, Genistein (GCP), Green Tea Extract, IM-862, ImmTher, Interferon alpha, Interleukin-12, Iressa (ZD1839), Marimastat, Metastat (Col-3), Neovastat, Octreotide, Paclitaxel, Penicillamine, Photofrin, Photopoint, PI-88, Prinomastat (AG-3340), PTK787 (ZK22584), RO317453, Solimastat, Squalamine, SU 101, SU 5416, SU-6668, Suradista (FCE 26644), Suramin (Metaret), Tetrathiomolybdate, Thalidomide, TNP-470, and Vitaxin.
- 29. (Amended) The method according to <u>claim 1</u> [any one of claims 1-11, 19-20, or 23-26], wherein said sample is a blood sample.
- 30. (Amended) The method according to <u>claim 1</u>[any one of claims 1-11, 19-20, or 24-27], wherein said sample comprises a peripheral blood mononuclear cell.
- 31. (Amended) The method according to <u>claim 1</u>[any one of claims 1-11, or 19-30], wherein said expression product comprises one of a TIE 1 sequence, a Salioadhesion or Siglec 1 sequence, a sequence as depicted in Figure 8 or Figure 17, or a part of analogue thereof.
- 37. (Amended) A method of determining whether a treatment is effective in changing the status of a certain set of target cells in an individual and/or altering an angiogenic process in an individual, said method comprising:

providing the diagnostic kit according to claim 35 [or 36];

obtaining a sample from said individual; and

detecting the presence of an expression product of at least one marker gene in said sample.

38. (Amended) A method of determining whether an individual possesses a tumor cell and/or a site of angiogenesis, said method comprising: providing the diagnostic kit according to claim 35[or 36]; obtaining a sample from said individual; and quantifying an expression product of at least one marker gene in said sample.